

§ 112 Rejection

Applicant has redrafted claim 27 to depend from claim 28. We thank the Examiner for the courtesy of his suggestions.

§ 102 Rejection

Claims 27 and 28 are rejected under 35 U.S.C. § 102(b) as being anticipated by Downs, et al. for reasons of record. The Examiner has characterized the Downs reference on page 3 as teaching "isolating allantoic tissue, culturing the tissue *in vitro*, transplanting the allantoic tissue to an embryo and observing the allantois, specifically observing the attachment of allantois to the chorion." The Examiner asserts that "treating allantoic tissue with a compound as claimed is equivalent to contacting the allantoic tissue with an embryo, as taught by Downs."

The Examiner also characterizes the Downs reference as treating "the allantoises with [<sup>3</sup>H]methyl thymidine . . . and observing the effect of [<sup>3</sup>H]methyl thymidine on growth and development . . . ."

The Examiner correctly characterizes our argument as being that the Downs reference "did not observe vascularization after administering [<sup>3</sup>H]methyl thymidine." In light of the Examiner's comments at the top of page 4, Applicant notes that they did not mean to indicate that "[<sup>3</sup>H]methyl thymidine prevented vascularization."

Applicant means to make the point that vascularization was not observed because Applicant was evaluating union of the allantois with the chorion and was evaluating neither growth nor vascularization. The point of the Downs reference was to begin to discover how the allantois fused with the chorion.

Applicant would like to make an additional point about the use of [ $^3\text{H}$ ] methyl thymidine in the Downs reference. For the experiments in the Downs reference, transplantation was carried out. All transplantations require that donor tissue be distinguishable from hosts. At the time, the preferred method for doing this was through labeling cells in S-phase of the cell cycle with [ $^3\text{H}$ ] methyl thymidine. Labeling cells in S-phase is not an accepted measure of cell growth, i.e., indicative of an increase in cell number or cell multiplication. However, just because a cell can be labeled during S-phase does not mean that the cell is going to divide. Many cells endoreduplicate their DNA in the absence of cell division. Thus, donor allantoises were distinguishable from host allantoises by means of a radioactive label in their chromosomes. These labeled allantoises were introduced into the exocoelom of hosts. Thus, tritium was applied to whole donor conceptuses only with the goal of being able to distinguish donor

allantoises from host allantoises after transplantation by autoradiographic methods.

Labeling with [<sup>3</sup>H] had to do with growth and development only insofar as to ensure that labeling whole conceptuses with a radioactive compound was not toxic to the donor conceptus. If growth and development of the labeled conceptus were compromised, Downs, et al. could not have carried out these transplantation experiments because the donor allantoic tissue would have been unhealthy and not provided a normal read-out for when fusion occurred.

The Examiner concludes that

"Applicants argue Downs does not teach observing vascularization as claimed. Applicant's arguments are not persuasive because observing growth of allantoic tissue is 'observing vascularization,' because allantoic tissue becomes the umbilical chord which have blood vessels, and because attachment to the allantois to the chorion [is] a step in the process of vascularization of the allantois."  
(Bracketed material added)

As far as vascularization is concerned, Downs, et al. only noted that remnant host allantoises contained blood vessels. Because these remnants had not fused with the chorion, Downs, et al. could only conclude that contact with the chorion was not necessary to vascularize the allantois. However, noting that the remnant allantois contained blood vessels does not indicate that the allantois vascularizes on its own. Those blood vessels in the remnant allantois could have been

introduced into the allantois by blood vessel invasion (angiogenesis) from the adjacent yolk sac, which is a well known vascular organ, and/or from the fetus.

In summary, when Downs, et al. was published, all one could conclude was that (i) the allantois fused with the chorion at a particular time in fetal development (beginning at 3-4-somite pairs), (ii) fusion involved only the allantois and the chorion, as donor allantoises did not generally fuse with other surfaces in the cavity, even though they had ample opportunity to do so, (iii) fusion was dependent upon the developmental maturity of the allantois, and (iv) introduction of blood vessels into the allantois did not seem to be dependent upon contact with the chorion. The reference did not address where those blood vessels came from, whether the allantois made them itself by differentiation of its mesoderm or by invasion from the yolk sac and/or fetus, both of which are connected to the allantois.

Applicant reiterates, as noted in the previous Office Action and in the Declaration of Karen Downs, that the Downs reference does not address when allantoic vascularization began and whether the chorion was required for allantoic vascularization. In fact, Applicant has demonstrated in later work that chorion is not required for allantoic vascularization. (Please see Declaration of Karen Downs, January 7, 2002.) Applicant

has clearly provided claim limitations (e.g., "(d) observing the vascularization . . ." and "alteration in the vascularization of the allantoic tissue . . .") that are not present in the Downs reference. It is Applicant's specification that would teach one of skill in the art how to observe and evaluate vascularization and whether vascularization was present at all. The Downs reference cannot and does not provide this information.

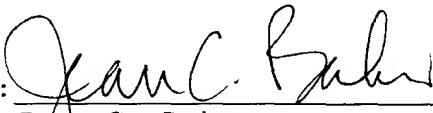
Applicants note that the specification describes criteria and procedures for observing vasculogenesis and that these criteria and procedures are not present in the Downs, et al. reference.

Applicant has enclosed a Petition and Fee for Two Months Extension of Time and believe that no further fees are necessary. However, if a fee is necessary, Applicant asks that it be charged to Deposit Account 17-0055.

Respectfully submitted,

Karen M. Downs

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**MARKED UP VERSION OF THE CLAIM**

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27. (Amended) The method of claim [25] 28 wherein  
the test compound is a protein.